

REMARKS/ARGUMENTS

Claims 1, 2, 4 to 8 and 13 are pending in the application. Claims 1, 2 and 7 have been amended, without prejudice. No claims are added or canceled.

Claims 1 and 2 have been amended by deleting reference to  $R^{2c}$  and  $R^{2d}$  forming a heterocyclic ring having 0-3 heteroatoms selected from O, N or S. Claim 1 has also been amended by expanding the provisos beyond the previously specified *ortho* and *para* isomers. Claims 2 and 7 have been amended by addition of a proviso that when  $R^2$  is  $CO_2Et$  and  $R^3$  is Ph,  $R^1$  is not H. The amendments will be discussed in greater detail below.

In the Office Action dated December 18, 2002, Claims 1, 2 and 7 stood rejected. Claims 4 to 6, 8 and 13 were objected to as dependent on a rejected base claim. Reconsideration of these rejections in view of the amendments and remarks to follow is respectfully requested.

***Claim 1***

In the Office Action, the Examiner maintained his position that the expression in regard to  $R^{2c}$  and  $R^{2d}$  forming a heterocyclic ring "cannot be allowed." See Office Action at p. 2. While applicants respectfully disagree with this rejection, for the reasons, for example, stated in the response submitted on October 24, 2002, in the interest of advancing prosecution of this application, this term has been deleted from Claim 1.

The Examiner also rejects Claim 1 on the basis that the terms "aryl" and "heteroaryl" are unclear. Applicants respectfully traverse this rejection. As clearly set forth in the claim, the term "aryl" includes moieties "selected from phenyl, naphthyl, indanyl and indenyl, each aryl being substituted with 0-5 substituents independently selected at each occurrence from  $C_{1-6}$  alkyl,  $C_{3-6}$  cycloalkyl, methylenedioxy,  $C_{1-4}$  alkyloxy- $C_{1-4}$  alkyloxy,  $-OR^{2m}$ , Br, Cl, F, I,

$C_{1-4}$  haloalkyl, -CN, -NO<sub>2</sub>, -SH, -S(O)<sub>n</sub>R<sup>2n</sup>, -COR<sup>2m</sup>, -CO<sub>2</sub>R<sup>2m</sup>, -OC(O)R<sup>2n</sup>, -NR<sup>2g</sup>COR<sup>2m</sup>, -N(COR<sup>2m</sup>)<sub>2</sub>, -NR<sup>2g</sup>CONR<sup>2o</sup>R<sup>2p</sup>, -NR<sup>2g</sup>CO<sub>2</sub>R<sup>2h</sup>, -NR<sup>2o</sup>R<sup>2p</sup> and CONR<sup>2o</sup>R<sup>2p</sup>," unless a more restrictive definition is provided elsewhere in the claim, with reference to specific variables.

*See supra*, p. 7. With regard to the Examiner's comment that the terms indanyl or indenyl are not usually considered to be "aryl," it is noted that an applicant is permitted to be his own lexicographer, provided that the usage is not repugnant to the usual and understood meaning of the term. Since, as specifically stated by the Examiner, the term "aryl" has multiple different definitions, *see* Office Action, p. 8, citing *In re Sus*, 134 U.S.P.Q. 301, the inclusion of indanyl and indenyl moieties within the generic "aryl" cannot be considered to be repugnant. In addition, since the Applicants have provided a specific definition of "aryl" within the claim, albeit one which may arguably include compounds that may not necessarily fall within every possible definition of the term, there can be no uncertainty regarding Applicants' intended meaning for the term.

Similarly, a definition for the term "heteroaryl" is also provided in Claim 1, and applies to any usage of the term in the claim, unless a narrower definition is otherwise provided for a specific substituent. As seen at pages 7 to 8 above, the term "heteroaryl" includes moieties selected from the group pyridyl, pyrimidyl, triazinyl, furanyl, quinolinyl, isoquinolinyl, thienyl, imidazolyl, thiazolyl, indolyl, pyrrolyl, oxazolyl, benzofuranyl, benzothienyl, benzothiazolyl, benzoxazolyl, isoxazolyl, triazolyl, tetrazolyl, indazolyl, 2,3-dihydrobenzo-furanyl, 2,3-dihydrobenzothienyl, 2,3-dihydro-benzothienyl-S-oxide, 2,3-dihydrobenzothienyl-s-dioxide, indolinyl, benzoxazolin-2-on-yl, benzodioxolanyl and benzodioxane, each heteroaryl being substituted at 0-4 carbon atoms with a substituent independently selected at each occurrence from the group C<sub>1-6</sub> alkyl, C<sub>3-6</sub> cycloalkyl, Br, F, I,

C<sub>1-4</sub> haloalkyl, -CN, NR<sup>2g</sup>R<sup>2h</sup>, nitro, -OR<sup>2m</sup>, -SH, -S(O)<sub>n</sub>R<sup>2n</sup>, COR<sup>2m</sup>, -CO<sub>2</sub>R<sup>2m</sup>, -OC(O)R<sup>2n</sup>, -NR<sup>2g</sup>COR<sup>2m</sup>, -N(COR<sup>2m</sup>)<sub>2</sub>, -NR<sup>2g</sup>CONR<sup>2o</sup>R<sup>2p</sup> and each heteroaryl being substituted at any nitrogen atom with 0-1 substituents selected from the group R<sup>2g</sup>, CO<sub>2</sub>R<sup>3a</sup>, COR<sup>3a</sup> and SO<sub>2</sub>R<sup>3a</sup> wherein, R<sup>3a</sup> is selected from the group C<sub>1-6</sub> alkyl, C<sub>1-4</sub> cycloalkyl-C<sub>1-6</sub> alkyl and benzyl, each benzyl being substituted on the aryl moiety with 0-1 substituents selected from the group C<sub>1-4</sub> alkyl, Br, Cl, F, I, C<sub>1-4</sub> haloalkyl, nitro, C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> haloalkoxy, and dimethylamino. Applicants respectfully submit that since the meaning of the term is clearly set forth, the term is not indefinite.

In view of the foregoing, Applicants respectfully submit that Claim 1 is not indefinite, and respectfully request that the Examiner withdraw his rejections in this regard.

It is further stated in the Office Action that the compounds defined by Claim 1 would be obvious in view of the compounds excluded by the provisos appearing at the end of the claim. Applicants also respectfully traverse this rejection. However, in the interest of advancing prosecution of this application, Applicants have broadened certain of the provisos, thereby increasing the number of compounds excluded. Specifically, Applicants have amended provisos (a) and (f) through (i) of Claim 1, so that reference to specific *ortho* or *para* isomers is removed.

With regard to the potential obviousness of the claimed compounds in view of the remaining excluded compounds, Applicants respectfully reiterate the arguments set forth in the response dated October 24, 2002, and respectfully assert that the Examiner has failed to establish the *prima facie* obviousness of the claimed compounds. It is well established that the prior art relied upon in making a rejection under 35 U.S.C. § 103, must contain some suggestion or incentive that would have motivated the skilled artisan to modify a reference or

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to combine references. *In re Fine*, 5.U.S.P.Q.2d 1596, 1598 (Fed. Cir. 1988). It is asserted in the Office Action that the motivation to modify the structurally similar compounds set forth in the provisos, to provide the compounds defined by Claim 1 derives from the expectation of one skilled in the art that such compounds will have similar properties. However, the references disclosing the compounds excluded by the provisos fail to indicate that the compounds possess any CRF antagonistic properties. For example, the compounds described in U.S. Patent No. 3,910,907, and the closely related compounds described in the *J. Med. Chem.* 1982, 25, 243-249 article, both cited in the specification at page 24, are said to be useful as *phosphodiesterase inhibitors*, not as CRF antagonists. Where the prior art does not teach the utility asserted for the claimed compounds, both the motivation and expectation of success for making *any* structural modifications to the cited compounds dissipates. *See In re Lahu*, 223 U.S.P.Q. 1257, 1259 (Fed. Cir. 1984) (in finding no motivation to modify a reaction intermediate to obtain a structurally similar compound, the court framed the issue as requiring an inquiry into whether the prior art "would suggest an unexpected property of the claimed compounds" or whether the prior art discloses any utility of its compounds that "would support an expectation that the claimed compounds would have similar properties"); *see also In re Stemniski*, 170 U.S.P.Q. 343, 347 (CCPA 1978) (where the prior art discloses no utility for disclosed compounds, no motivation will be inferred to make the structural change needed to arrive at the claimed compounds). Moreover, Applicants note that the practice of using provisos to exclude specific structurally similar compounds that may have been described for unrelated usages is a well established practice, that has long been sanctioned by the courts.

Accordingly, Applicants respectfully submit that the claimed compounds are not *prima facie* obvious over the specific compounds excluded by the provisos, particularly, in view of the amendments made herein, and respectfully request that the rejection under Section 103 be reconsidered and withdrawn. There being no further rejections pending with regard to this claim, an allowance of Claim 1 is respectfully requested.

***Claim 2***

Claim 2 stands rejected as being indefinite for the same reasons as Claim 1. As was done with regard to Claim 1, Applicants have amended Claim 2 to delete reference to R<sup>2c</sup> and R<sup>2d</sup> forming a heterocyclic ring. Applicants also note that definitions for the terms "aryl" and "heteroaryl" are specifically provided in Claim 2 (*see supra*, p. 15), and these definitions apply to any usage of the terms in this claim, unless a narrower meaning is provided elsewhere in the claim, with regard to a particular substituent. Accordingly, Applicants respectfully assert that Claim 2 is not indefinite, and request that this rejection be withdrawn.

It is not clear in the Office Action whether the compounds defined by Claim 2 are also considered to be obvious over the compounds excluded by the provisos in Claim 1. However, to the extent that such a rejection was intended, Applicants respectfully traverse. It is noted that all of the provisos in Claim 1 are addressed to compounds in which the variable R<sup>2</sup> is H, CN, CO<sub>2</sub>Et, or one of the halogens Cl or Br. In Claim 2, however, H, CN and halogens are not possible substituents for the variable R<sup>2</sup>. Accordingly, the compounds of Claim 2 define over the compounds described in the provisos of Claim 1, *inter alia*, for the reasons set forth with regard to Claim 1.

While CO<sub>2</sub>Et is a possible substituent for the variable R<sup>2</sup> in Claim 2, the compounds described in the prior art have been specifically excluded by the proviso that has been added

to Claim 2 by the instant amendment. Specifically, U.S. Patent 3,910,907 describes compounds said to have phosphodiesterase inhibitory properties in which  $R^2$  is  $CO_2Et$  and  $R^3$  is Ph, and  $R^1$  is H, Ph,  $CH_3-C_6H_4$ , or  $CH_3O-C_6H_4$ . Of these, only H is a possible substituent for  $R^1$  in Claim 2. Thus, compounds in which  $R^2$  is  $CO_2Et$ ,  $R^3$  is Ph, and  $R^1$  is H have been specifically excluded by the added proviso. As discussed above with regard to Claim 1, since the '907 patent does not contain any teaching or suggestion that the compounds described therein may be used as CRF antagonists, one of ordinary skill in the art would have no motivation to modify the described compounds to include the other  $R^1$  substituents set forth in Claim 2. Accordingly, Applicants respectfully submit that the compounds of Claim 2 define over that reference.

There being no further rejections pending with regard to this claim, an allowance of Claim 2 is respectfully requested.

**Claim 7**

The basis for rejection of Claim 7 is not clearly stated in the Office Action. However, to the extent that the claim is rejected for the reasons applied to Claims 1 and 2, the rejection is respectfully traversed.

It is noted that Claim 7 as originally drafted does not contain the reference to  $R^{2c}$  and  $R^{2d}$  forming a heterocyclic ring that was objected to. Moreover, the terms "aryl" and "heteroaryl" are specifically defined in Claim 7 (*see supra*, pp. 19-20), and these definitions would apply to any usage of the term in the claim, unless a narrower definition is provided elsewhere in the claim with regard to any specific substituent. Moreover, the proviso that was added to Claim 2, as discussed previously, has been added to Claim 7, as well, to more clearly distinguish the prior art.

DOCKET NO.: PH-7094-A (BMS-0875)  
Application No.: 09/990,138  
Office Action Dated: December 18, 2002

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Accordingly, it is respectfully submitted that any pending rejections of Claim 7 have been overcome, and an allowance of the claim is requested respectfully.


***Claims 4 to 6, 8 and 13***

The Examiner has already indicated that Claims 4 to 6, 8 and 13 define patentable subject matter, but were objected to as dependent upon a rejected base claim. However, as set forth above, it is respectfully asserted that the base claims are in condition for allowance. Accordingly, an allowance of Claims 4 to 6, 8 and 13 is respectfully requested, as well.

There being no further issues noted in the Office Action, it is believed that the application is now in condition for allowance. Accordingly, a Notice of Allowance of Claims 1, 2, 4 to 8 and 13 is respectfully requested. If the Examiner is of a contrary view, Applicants respectfully request that the Examiner telephone their undersigned representative at the number below. Applicants note, however, that all written correspondence for this application should continue to be sent to:

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Date: May 19, 2003

  
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